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FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

EXAMINER

VENCI, DAVID J

ART UNIT PAPER NUMBER

1641

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/715,329	Applicant(s) ZHAO ET AL.	
	Examiner David J. Venci	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 8, 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 8, 10 and 30-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9 and 11-29 is/are rejected.
- 7) ☒ Claim(s) 25-27 is/are objected to.
- 8) ☒ Claim(s) 1-32 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restrictions

Examiner acknowledges Applicant's election of Group I, claims 1-29, without traverse, in the reply filed on March 8, 2005. Examiner further acknowledges Applicant's election of azidoprenyl/farnesyl diphosphate species, readable on claims 1-7, 9 and 11-29, without traverse.

Claims 30-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Claims 8 and 10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Currently, claims 1-7, 9 and 11-29 are under examination.

Specification

The disclosure is objected to because of the following informalities:

On page 11, line 27, the recitation of "equation 1, herein above" is indefinite because equation 1 does not appear above.

On page 18, scheme 1, the depiction of "+" adjacent to various chemical structures is indefinite because it is not clear what chemical entity corresponds or correlates to "+".

On page 24, scheme 4, the depiction of "+" adjacent to various chemical structures is indefinite because it is not clear what chemical entity corresponds or correlates to "+".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-7, 9 and 11-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step (a), the recitation of "isoprenyl azide substrate of at least a first protein" is grammatically awkward and is indefinite because it is not clear whether said "substrate" describes a substrate for said "azide" entity, or whether said "substrate" describes a substrate for said "protein" entity. In addition, it is not clear whether step (a) requires obtaining a first protein and/or a cell. In addition, the recitation of "a first protein" is indefinite because it is not clear whether "a first protein" corresponds to "a first isoprenylated protein" recited in the preamble.

In claim 1, step (b), the recitation of "a first azide" is indefinite because it is not clear whether "a first azide" corresponds to the "isoprenyl azide" of step (a), or whether "a first azide" describes a separate azide entity distinct from the "isoprenyl azide" of step (a). In addition, the recitation of "incorporates into the protein at least a first azide from the substrate" is indefinite because it is not clear whether "a first azide" is incorporated into the protein, or whether both "a first azide" and "substrate" are incorporated into the protein. It is not clear whether "a first azide" and "substrate" are separate entities, or how "a first azide" and "substrate" become separate entities. In addition, the recitation of "contacting the cell" is indefinite because it is not clear what entity is contacted with the cell. In addition, the recitation of "the protein" lacks antecedent basis and is indefinite because it is not clear whether "the protein" corresponds to "a first protein" recited in step (a) or "a first isoprenylated protein" recited in the preamble. In addition, the recitation of "the substrate" lacks antecedent basis and is indefinite because it is not clear whether "the substrate" corresponds to "a synthetic isoprenyl azide substrate" recited in step (a).

In claim 1, step (c), the recitation of "proteins produced by said cell with a phosphine capture reagent" is indefinite because it is not clear how cells produce proteins "with a phosphine capture reagent." It is not clear whether the cell is contacted with "a phosphine capture reagent," or whether the cell produces "a

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phosphine capture reagent" endogenously. In addition, the recitation of "proteins produced by said cells... by the Staudinger reaction" is indefinite because it is not clear how cell produce proteins by performing "the Staudinger reaction." In addition, the recitation of "detecting at least said first protein... with a phosphine capture reagent" is indefinite because it is not clear whether said first protein is contacted with a phosphine moiety, or whether said first protein is produced with a phosphine moiety by said cell. In addition, the recitation of "said first protein" is indefinite because it is not clear whether "said first protein" corresponds to "the protein" recited in step (b) or "a first isoprenylated protein" recited in the preamble.

Claim 1 is further rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The preamble of claim 1 does not appear to correspond to the method outcome. Specifically, the preamble recites a method for detecting "a first isoprenylated protein." However, final step (c) recites the step of detecting "said first protein." It is not clear how merely detecting "said first protein" amounts to detecting "a first isoprenylated protein." It is not clear whether "said first protein" corresponds to "the protein" recited in step (b) or "a first isoprenylated protein" recited in the preamble. It is not clear whether additional method steps are required to detect "a first isoprenylated protein." Clarification is required.

In claim 2, the recitation of "the protein is farnesylated" is indefinite because it is not clear during which step(s) of claim 1 said protein is farnesylated.

In claims 4-6, the recitation of "FPP" lacks antecedent basis. In addition, the recitation of "FPP is inhibited" is indefinite because the physical parameters underlying the process of inhibition, as well as the standard or degree of inhibition required by "inhibited" is not clear. It is not clear how "HMG Co-A reductase inhibitor" and "lovastatin" inhibit FPP.

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In claim 12, it is not clear how "Western blot analysis" is incorporated into the method of claim 1. It is not clear whether "Western blot analysis" is performed in addition to step (c).

In claim 19, it is not clear how "affinity-purification" is incorporated into the method of claim 1. It is not clear whether "affinity-purification" is performed in addition to step (c).

In claim 20, the recitation of "a bead" is indefinite because it is not clear whether a single bead is intended.

In claim 21, it is not clear how "a nucleophile" is incorporated into the method of claim 1 or whether "a nucleophile" correlates to any entity recited in claim 1.

In claim 24, the recitation of "the prenylated protein" lacks antecedent basis.

In claims 25-26, the incorporation of "+" adjacent to the recited molecular formulas is indefinite because it is not clear what chemical entity corresponds or correlates to "+".

In claim 28, step (a) is grammatically awkward and is indefinite because it is not clear whether "a synthetic substrate" comprises "a first azide", or whether "said protein" comprises "a first azide."

In claim 29, the recitation of "synthetic" is indefinite because it is not clear how a prenylated substrate (e.g. a prenylated protein) is "synthetic." In addition, it is not clear how a prenylated substrate is incorporated into the method of claim 28. It is not clear how a prenylated substrate is "incorporated into the protein."

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Spielmann et al. (US 6,284,910).

Spielmann et al. teach a method for labeling a protein (see col. 27, lines 14-15, "H-Ras farnesyl-group") in a cell (see col. 27, line 12, "oocytes") comprising the steps of: obtaining a synthetic substrate of said protein (see col. 27, line 17, "farnesyl analogs") comprising an azide (see col. 6, line 52, "N₃"), and contacting the cell under conditions wherein the synthetic substrate is taken up (see col. 27, line 18, "microinjection") and incorporates (see col. 27, lines 16-17, "enzymatic methods to attach") into the protein (see col. 27, line 17, "H-Ras") and wherein the protein is labeled with said first azide (see col. 27, lines 14-15, "H-Ras farnesyl-group").

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9, 11, 13 and 15-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spielmann et al. (US 6,284,910) in view of Saxon & Bertozzi (US 6,570,040).

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Spielmann et al. teach a method for detecting an isoprenylated protein (see col. 27, lines 14-15, "H-Ras farnesyl-group") in a cell (see col. 27, line 12, "oocytes") comprising the steps of: obtaining a synthetic isoprenyl (see col. 27, line 17, "farnesyl analogs") azide (see col. 6, line 52, " N_3 ") substrate of a protein (see col. 26, line 3, "FTase"), contacting the cell under conditions wherein the cell takes up (see col. 27, line 18, "microinjection") and incorporates (see col. 27, lines 16-17, "enzymatic methods to attach") into the protein (see col. 27, line 17, "H-Ras") a first azide (see col. 6, line 52, " N_3 ") from the substrate (see col. 27, line 17, "farnesyl analogs"), and detecting (see col. 25, line 66, "Assay for Analog Transfer") said protein (see col. 26, line 3, "FTase").

Spielmann et al. do not teach "a phosphine capture reagent" or "the Staudinger reaction".

However, Saxon & Bertozzi teach the use of a phosphine capture reagent and the Staudinger reaction for detecting intracellular azido-target substrates (see col. 14, line 57, "detectable labels", line 55, "intracellular", lines 52-53, "azido-target substrate"). Therefore, it would have been obvious for a person of ordinary skill in the art to perform the method for detecting an isoprenylated protein, as taught by Spielmann et al., with a phosphine capture reagent and the Staudinger reaction because Saxon & Bertozzi discovered that the Staudinger reaction is both selective and compatible with aqueous environments, which allows for *in vivo* applications (see Abstract).

With respect to claim 3, Spielmann et al. teach a method wherein the first protein is isolated (see sentence bridging cols. 21-22).

With respect to claims 4-6, Spielmann et al. teach a method wherein FPP is inhibited with lovastatin (see col. 27, line 49, "mevinolin").

With respect to claims 7 and 9, Spielmann et al. teach a method comprising an azido farnesyl diphosphate (see col. 27, line 35, "FPP analogues", col. 6, line 52, " N_3 ").

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With respect to claim 11, Spielmann et al. teach a method wherein the first protein is native to said cell (see col. 27, line 32, "FTase in oocytes").

With respect to claims 13 and 20, Saxon & Bertozzi teach a method wherein the phosphine is bound to a solid support comprising an inorganic bead (see col. 17, line 28).

With respect to claims 15-16, Saxon & Bertozzi teach a method wherein the phosphine comprises a fluorescent label (see col. 16, lines 55-67).

With respect to claims 17-19, Saxon & Bertozzi teach a method wherein the phosphine comprises biotin reaction with avidin (see col. 15, lines 8-9).

With respect to claims 21-22, Saxon & Bertozzi teach a method wherein a nucleophile is immobilized on a polysaccharide (see col. 13, lines 4-5).

With respect to claim 23, Spielmann et al. teach a method wherein the synthetic prenyl azide substrate is a substrate for a plurality of proteins (see col. 1, lines 59-67, "FTase", "CAAX GGTase", "Rab GGTase").

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Spielmann et al. (US 6,284,910) and Saxon & Bertozzi (US 6,570,040) as applied to claim 1, and further in view of Lodish et al., MOLECULAR CELL BIOLOGY, 4th ed., W.H. Freeman & Co. (1999).

Spielmann et al. and Saxon & Bertozzi teach a method for detecting an isoprenylated protein as substantially described supra. The aforementioned references do not teach Western blot detection.

However, Lodish et al. teach the use of Western blot detection for detecting a particular protein in a complex mixture (see Section 3.5). Therefore, it would have been obvious for a person of ordinary skill in the art to perform the method for detecting an isoprenylated protein, as taught by Spielmann et al. and Saxon & Bertozzi, with Western blot detection because Lodish et al. teach Western analysis is "one of the most powerful methods for detecting a particular protein" combining "superior resolving power of gel electrophoresis, the specificity of antibodies, and the sensitivity of enzyme assays."

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Spielmann et al. (US 6,284,910) and Saxon & Bertozzi (US 6,570,040) as applied to claims 1 and 13, and further in view of Holmes, 62 J. ORG. CHEM. 2370 (1997).

Spielmann et al. and Saxon & Bertozzi teach a method for detecting an isoprenylated protein as described supra. In addition, Saxon & Bertozzi teach the use of a cleavable linker (see Abstract). The aforementioned references do not teach the use of a photocleavable linker.

However, Holmes teaches the use of a photocleavable linker for anchoring biomolecules to solid supports (see Abstract). Therefore, it would have been obvious for a person of ordinary skill in the art to replace the cleavable linker of Saxon & Bertozzi with a photocleavable linker because Holmes states that photocleavable linkers are "particularly attractive in combinatorial library screening," as they result in biomolecules that are free of cleavage reagents (see p. 2370, col. 1, lines 11-18).

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Allowable Subject Matter

Claims 25-27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter:

Claims 25-27 recite specific isoprenyl azide compounds used as labels in a method of detecting isoprenylated proteins. The compounds of claims 25-27 are acyclic aliphatic compounds. Spielmann et al. (US 6,284,910) also teach the use isoprenyl azide compounds for detecting farnesylation (see *supra*, *Claim Rejections - 35 USC § 103*). However, the isoprenyl azide compounds of Spielmann et al. do not appear to be acyclic aliphatic compounds. As evidenced by the STIC Search Report, submitted herewith this Office Action, the prior art does not appear to teach or suggest the specific acyclic aliphatic compounds listed in claims 25-27. Therefore, claims 25-27 appear to be free of the cited prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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David J Venci
Examiner
Art Unit 1641

djv



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

04/01/05